

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: )  
 )  
Claude NÉGRIER et al. )  
 )  
Serial No.: Unassigned ) Group Art Unit: Unassigned  
 )  
Filed: Concurrently herewith ) Examiner: Unassigned  
 )  
For: MODIFIED FACTOR VIII cDNA )

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

**PRELIMINARY AMENDMENT**

Prior to the examination of the above application, which is a 37 C.F.R. § 1.53(b) divisional application of U.S. Ser. No. 09/526,935, now allowed, please amend this application as follows:

**IN THE CLAIMS:**

Please cancel claims 1-6. Please add claims 7-11 as follows:

7. A process for the production of Factor VIII protein comprising:
- a) preparing a modified Factor VIII cDNA comprising a deletion of the B-domain and insertion of the truncated Factor IX intron 1 (SEQ ID NO: 9) in one or more splice sites of the Factor VIII cDNA;
  - b) introducing the modified Factor VIII cDNA into a cell; and

c) expressing the modified Factor VIII cDNA in said cell to produce Factor VIII protein.

8. A process for the production of Factor VIII protein comprising:

- a) preparing a modified Factor VIII cDNA comprising a replacement of the B-domain with nucleotides encoding four arginines and insertion of the truncated Factor IX intron 1 (SEQ ID NO: 9) in one or more splice sites of the Factor VIII cDNA;
- b) introducing the modified Factor VIII cDNA into a cell; and
- c) expressing the modified Factor VIII cDNA in said cell to produce Factor VIII protein.

9. The process as claimed in claim 7, wherein at least one insertion site of the truncated Factor IX intron 1 is chosen from Factor VIII intron 1 splice site, Factor VIII intron 12 splice site, and Factor VIII intron 13 splice site.

10. The process as claimed in claim 8, wherein at least one insertion site of the truncated Factor IX intron 1 is chosen from Factor VIII intron 1 splice site, Factor VIII intron 12 splice site, and Factor VIII intron 13 splice site.

11. A process for producing a protein comprising:

- a) obtaining a wildtype cDNA of the protein;
- b) introducing splice sites into the wildtype cDNA;
- c) preparing a modified cDNA by inserting one or more introns from one or more additional cDNAs into the wildtype cDNA;
- d) introducing the modified cDNA into a cell; and

e) expressing the polypeptide encoded by the modified cDNA in the cell to produce the protein,  
wherein the yield of the protein produced with modified cDNA is greater than the yield produced with wildtype cDNA.

**REMARKS**

Upon entry of this amendment, claims 1-6 are deleted and claims 7-11 are added. No new matter has been added.

If there is any fee due in connection with the filing of this Preliminary Amendment, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,  
GARRETT & DUNNER, L.L.P.

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Dated: June 15, 2001